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TITLE: A Placebo-Controlled Augmentation Trial of Prazosin for Combat Trauma PTSD

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14. ABSTRACT

This study consists of a 14-week, two parallel group, randomized placebo controlled trial to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist, prazosin, for reducing trauma nightmares and sleep disturbance and improving global function and sense of well-being, in 210 OIF and OEF combat-exposed returnees with PTSD and persistent raumarelated nightmares and disrupted sleep. A secondary aim is to assess efficacy of prazosin for reducing total PTSD symptoms, reducing symptoms of depression, improving quality of life, and reducing alcohol craving.

15. SUBJECT TERMS
PTSD, prazosin, trauma nightmares, sleep

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Introduction

The primary objective of this randomized, double-blind, placebo-controlled trial is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin compared to placebo for combat stress-related nightmares, sleep disturbance, and overall function in trauma-exposed service members. The secondary objective of this trial is to assess the efficacy of prazosin for reducing total PTSD symptoms, reducing symptoms of depression, improving quality of life, and reducing alcohol use.

210 male and female returning troops from Operation Iraqi or Enduring Freedom (OIF/OEF), who manifest persistent combat stress-related nightmares and sleep disturbance, will be enrolled in the study. Participants will undergo a flexible dose titration period followed by optimal dose treatment for a total of 15 weeks including the titration period. Primary and secondary outcome measures will assess nightmares, sleep disturbance, other stress-related symptoms, depression, global function, and quality of life and will be administered every four weeks. Data will be analyzed for significant differences among treatment groups using generalized estimating equations.

Body

We are happy to report that all regulatory approvals have been received at VA Puget Sound and Walter Reed AMC, including HRPO approval and conditional approval (as of 6/23/09) has been received from the Madigan AMC IRB (estimated complete approval by 7/15/09). Given that our recruitment mechanisms and contacts are in place at all sites, we anticipate entering two subjects per week into the trial beginning 7/6/09 at Walter Reed AMC and VA Puget Sound and 8/1/09 at Madigan AMC.

Beginning July 2009 at Walter Reed AMC and VA Puget Sound, and August 2009 at Madigan AMC, we will screen at least 5 potential eligible OIF/OEF returnees weekly at each site to enable us to enter at least 2 appropriate and consented subjects at each site per month (total 6 per month across all sites). With final approval at VA Puget Sound received, ten potential subjects have been scheduled for screening the first week after the July 4th weekend.

Key Research Accomplishments

- Protocol, consent form, and study materials approved by regulatory bodies.
- CRADA between CIRO, DCI, and HJF prepared and ratified (Walter Reed AMC).
- Study materials, including eligibility, baseline, and follow-up assessments developed, approved, and ready for assembly.
- Study ready to begin recruitment and enrollment of participants.

Reportable Outcomes

Pending

Conclusions

Pending

References

Raskind MA, Dobie DJ, Kanter ED, Petrie EC, Thompson CE, Peskind ER. The alpha1-adrenergic antagonist prazosin ameliorates combat trauma nightmares in veterans with posttraumatic stress disorder: a report of 4 cases. J Clin Psychiatry 2000 February;61(2):129-33.

Raskind MA, Peskind ER, Kanter ED, Petrie EC, Radant A, Thompson CE, Dobie DJ, Hoff D, Rein RJ, Straits-Troster K, Thomas RG, McFall MM. Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry 2003 February; 160(2):371-3.

Daly CM, Doyle ME, Radkind M, Raskind E, Daniels C. Clinical case series: the use of Prazosin for combat-related recurrent nightmares among Operation Iraqi Freedom combat veterans. Mil Med 2005 June;170(6):513-515.

Taylor FB, Lowe K, Thompson C, McFall MM, Peskind ER, Kanter ED, Allison N, Williams J, Martin P, Raskind MA. Daytime prazosin reduces psychological distress to trauma specific cues in civilian trauma posttraumatic stress disorder. Biol Psychiatry 2006 April 1;59(7):577-81.

Taylor FB, Martin P, Thompson C, Williams J, Mellman TA, Gross C, Peskind ER, Raskind MA. Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma posttraumatic stress disorder: a placebo-controlled study. Biol Psychiatry 2008 March 15;63(6):629-32.

Miller LJ. Prazosin for the treatment of posttraumatic stress disorder sleep disturbances. Pharmacotherapy 2008; 28(5):656-666.

Taylor HR, Freeman MK, Cates ME. Prazosin for treatment of nightmares related to posttraumatic stress disorder. Am J Health Syst Pharm 2008; 65(8):716-722.

Appendices
N/A

Supporting Data
Pending